the Examiner's rejections made in the July 5, 2001 Office Action have been overcome and respectfully request that the Examiner reconsider and withdraw same.

Pursuant to the requirements of 37 C.F.R. 1.121, applicants annex hereto as Exhibit A a copy of the amended claims marked up to show the changes made herein relative to the previous version thereof.

The Claimed Invention

This invention provides a method for determining the likelihood that a prostate carcinoma is aggressive. This invention also provides a method for determining the likelihood that a prostate hyperplasia is a benign prostate hyperplasia.

The instant methods are based on the *unexpected* discovery that both prostate carcinoma and benign prostate hyperplasia are *more likely than not* to be characterized by a reduced level of p27 protein.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1-3 under 35 U.S.C. §112, first paragraph, as allegedly not enabled.

In response, applicants respectfully traverse the Examiner's rejection.

Claim 1 provides a method for determining the likelihood that a prostate carcinoma is aggressive. This method comprises, in relevant part, determining whether the amount of p27 protein in the prostate carcinoma is reduced relative to the amount of p27 protein present in a normal prostate sample, a reduced amount indicating a likelihood that the prostate carcinoma is aggressive.

Claims 2 and 3 provide a method for determining the likelihood that a prostate hyperplasia is benign. This method comprises, in relevant part, determining whether the amount of p27 RNA in the prostate hyperplasia is reduced relative to the amount of p27 RNA present in a normal prostate sample, a reduced amount indicating a likelihood that the prostate hyperplasia is benign.

With respect to claim 1, the Examiner maintains, in essence, that the aggressiveness of a prostate carcinoma cannot be determined based "*solely* on the lack of expression of p27" (emphasis added). In support of her position, the Examiner cites data from the specification showing that the majority of, but not all, prostate carcinomas tested show reduced levels of p27.

Applicants maintain that the Examiner's position regarding the diagnosis of aggressive prostate carcinoma is inapposite to the enablement of claim 1. Again, this claim is directed to a method of determining the *likelihood* that a prostate carcinoma is aggressive. The very notion of determining this likelihood implies the possibility, however small, that a prostate carcinoma may in fact *not* be aggressive. This notion differs fundamentally from *diagnosing* aggressive prostate carcinoma, i.e., determining that a prostate carcinoma *is in fact* aggressive. It is irrelevant here whether the data set forth in the specification support a diagnostic method. Rather, these data show that if a prostate carcinoma is characterized by a reduced level of p27 *more often than not*, it is *more likely* aggressive than not. Thus, applicants maintain that the specification clearly supports the claimed method of determining a likelihood of aggressiveness, and that similar support for a method of diagnosis need not be shown.

It is noted that the Examiner's reliance on Lloyd, et al. is misplaced. This reference is cited as allegedly showing the inherent unpredictability regarding p27 levels and cancer *generally*, as exemplified by increased p27 levels in certain mammary cell lines. Assuming *arguendo* that Lloyd, et al. in fact teach such unpredictability in mammary cell lines, that teaching in no way affects the reliability of the prostate carcinoma data provided in this application. For this reason, the teachings of Lloyd, et al. have no bearing on the enablement of claim 1.

With respect to claims 2 and 3, the Examiner makes an assertion similar to that made concerning claim 1, i.e., that the benign nature of a prostate hyperplasia cannot be diagnosed based *solely* on whether the prostate hyperplasia is characterized by reduced p27 RNA. The Examiner also asserts that the specification does not provide sufficient guidance as to the meaning of the terms "appropriate sample" and "decrease."

Applicants traverse the Examiner's position regarding the diagnosis of benign prostate hyperplasia based on reduced p27 RNA levels, given that claims 2 and 3 instead provide a method for determining the *likelihood* of a prostate hyperplasia's being benign. The distinction between diagnosis and the determination of likelihood has already been addressed above.

Applicants also assert that one skilled in the art would know what the term "appropriate sample" means in the context of claims 2 and 3. As page 26, lines 30-35 make clear, "appropriate samples" of prostate hyperplasia include, by way of example, epithelial, stromal and fibromuscular cells in hyperplastic nodules. Hence, the specification provides sufficient guidance to practice this method. Likewise, the term "decrease" to one skilled in the art would be abundantly clear with respect to comparing levels of p27 RNA in

normal and diseased tissue. The Examiner's emphasis on an alleged lack of statistical significance between such numbers is besides the point given that this method is for determining the likelihood -- and not diagnosing -- a disorder.

In view of the above remarks, applicants maintain that claims 1-3 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 2 and 3 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner asserted that the phrase "appropriate sample" is unclear.

In response, applicants respectfully traverse the Examiner's rejection for the reasons set forth above in response to the rejection under 35 U.S.C. §112, first paragraph.

In view of the above remarks, applicants maintain that claims 1-3 satisfy the requirements of 35 U.S.C. §112, second paragraph.

Summary

In view of the amendments and remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number

provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Assistant Commissioner for Patents, Washington, D.C. 20231.

10/5/01

Alan J. Morrison
Reg. No. 37,399

Date